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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,447	11/17/2003	Edward Roberts	7567/80871	9363

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EXAMINER	
BERNHARDT, EMILY B	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/714,447	ROBERTS ET AL.	
	Examiner	Art Unit	
	Emily Bernhardt	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *12-15 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,16 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/836,830.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/17/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-11,16 and 18, drawn to compounds, compositions and use for treating pain where G=N and A and B are carbocyclic rings, classified in class 544, subclasses such as 393,396; class 514 subclass 255.04,etc.

II. Claims 1-11,16 and 18, drawn to compounds,compositions and use for treating pain where G=N and A=quinolinyl and B=carbocyclic, classified in class 544, subclass 363;class 514 subclass 253.06.

III. Claims 1-11,16 and 18, drawn to compounds,compositions and use for treating pain where G=N and A=benzofuranyl, B=carbocyclic, classified in class 544, subclass 379; class 514 subclass 254.11.

IV. Claims 1,2,4-11,16 and 18, drawn to compounds, compositions and use for treating pain where G=C and A/B rings are as defined for Group I, classified in class 546, subclasses such as 234; class 514 subclases 317,331,etc.

V. Claims 1,2,5-11,16 and 18, drawn to compounds,compositions and use for treating pain where G=C and A/B rings are as defined for Group II, classified in class 546, subclass 176;class 514 subclass 314.

VI. Claims 1,2,5-11, 16 and 18, drawn to compounds, compositions and use for treating pain where G=C and A/B rings are as defined for Group III, classified in class 546, subclass 196; class 514 subclass 320.

VII. Claims 1,2,3,5-11,16 and 18, drawn to other compounds,compositions and use for treating pain not provided for by I-VI above, classified in class 544/546, subclasses various as determined by the nature of A/B rings; class 514, various subclasses

VIII. Claims 12-13 , drawn to additional uses employing compounds of I-VII, classified in class 514, subclasses various.

IX. Claim 17, drawn to multiple processes for making compounds, classified in class 544/546, subclasses various as determined by ultimate final products being formed.

X. Claims 14 -15, drawn to radiolabelled compounds of I-VII and use as diagnostic agent, classified in class 544/546 and 435, subclasses various.

If VII is elected further election to G and A ring as was done for I-VI is required with B= heteroaromatics.

If VIII is elected applicants must select one use and a particular compound group.

If IX is elected a single process must be chosen for a particular compound group.

If X is elected a specific compound group must be chosen.

The inventions are distinct, each from the other because of the following reasons:

Compounds of I-VII are variously substituted on piperazine/piperidine rings which are classified separately and are not art-recognized equivalents such that a reference to one of the groups would necessarily apply to those remaining. Within elected group I are many differing issues of patentability.

Inventions I-VII and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case more than one use exists for compounds being claimed as evidenced by those being claimed and others shown in the art applied below

Inventions I-VII and IX are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that

the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case there are many processes for making instant compounds in addition to the two alternative one recited in claim 17. See for example Coker (EP'323).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Labelled compounds of X are separate inventions since they are particularly employed as diagnostic tools and not as pharmaceuticals. Art which may be pertinent to one or more of the compound groups would not necessarily be relevant to the subject matter of X which requires an additional search not needed for remaining uses.

During a telephone conversation with Mr. Sanzo on 8/12/04 a provisional election was made with right of traverse to prosecute the invention of I, claims 1-11,16 and 18. Affirmation of this election must be made by applicant in replying to this Office action. Claims 12-15 and 17 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The abstract of the disclosure is objected to because "comprising" on the 4th line does not read well. "Comprise" is grammatically correct.. Correction is required. See MPEP ' 608.01(b).

Claims 1-11, 16 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1.In the (iii) definition for A there are 2 bonds emanating from the phenyl rings depicted- one fixed and one floating. Thus its not clear how these rings are attached to the methylene carbon atached to G. See claims 1- 3.

2.In describing optional substituents for the A rings , a "substituent" following "ring of each A" in main claim 1 (p.93) appears extraneous and so should be deleted. Additionally, throughout the definitions for aryl and heteroaryl rings and B rings, hydrogen as a substituent is redundant since in the absence of any non-H substituents hydrogen is understood as being present.

3. "C1" alkenyl appears in several instances. See R1, R7, R8 definitions. One needs at least 2 carbons for such moieties.

4. "Heteroaryl having from 5-10 atoms" in the claims is unclear as to structural makeup? What is an example of such a heteroaromatic ring having for example 7 atoms? 8 atoms, etc. ?

5. "Naphtyl" is a misspelling throughout the claims including species in claim 4 .

6."Prodrugs" at the end of main claim 1 is unclear as to intended scope. Specification provides no guidance as to structural makeup except the mention of a textbook directed to the topic of prodrugs. Choice of derivatives as suitable prodrugs requires testing for rate of cleavage as well as *in vivo* stability and such is a function of the molecular structure of the parent drug and in the absence of any guidelines as to what may be suitable or what desired effect (eg. increased solubility) is to be achieved, one cannot readily determine intended scope.

7. Proviso at the end of claim 2 appears to be redundant since it is already recited in claim 1 from which 2 depends.

8.In claim 3 R7 and R8 are never "defined above" in this claim.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 6-11 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims drafted in terms of "use " have been held to be non-statutory. Note Clinical Products v. Brenner 149 USPQ 475.

Claims 1-11,16 and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

1."Isomers" at the end of main claim 1 includes position isomers. Inclusion of such would mean that A and B as well as R1 moieties could be at different locations on the piperazine ring other than at the fixed positions shown in formula (I). Such isomers would certainly have quite different properties and structure from that made and presumably tested. This rejection applies to claim 1 and claims dependent thereon.

2.Prodrugs as recited in the claims reads on all such functionalized derivatives regardless of complexity of structure for which there is no enabling disclosure how to use to yield the parent compound much less for treating pain. By definition prodrug forms are not active themselves yet method claims include such compounds.

3. Specification is not adequately enabled for the scope of piperazines claimed which can have a variety of functional groups including diverse heteroaryls as substituents on rings A,B as well as in the R variables. Compounds made (see claim 4) and presumably tested have one or two substituents on A,B rings such as alkoxy and halo groups with remaining variables being predominately H, methyl or allyl or cyclopropylmethyl. There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. In the absence of any test data showing structure-activity trends there is no reasonable assurance as to what type of heteroaromatics will work. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition. Thus given the breadth of the claims, the level of unpredictability in the art and the lack of direction (i.e. working examples) provided as to what other moieties might work, this rejection is being applied.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless □□

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,2,5,20,16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Chang (WO'51). Chang which published more than a year earlier from applicants' international filing date discloses anisole derivatives which read on the instant claims for treating among other uses, pain. See 2nd and 3rd last compounds on p.9 and corresponding examples 26 and 27. Note compound in eg.26 was further treated with HCl to generate the monohydrochloride salt.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was

made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-5,21,25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang (US'830 or WO'051). The US patent discloses compounds anticipated by WO'051 applied above which have an anisole ring corresponding to instant B and N-phenyl carboxamides as instant A. See compounds in col.8, lines 44-49. While compound claims rejected herein are not anticipated by Chang they are obvious variants since US Chang teaches not only N-phenylcarboxamides corresponding to instant A but also N-alkyl carboxamides such as N-diethylcarboxamides and salts thereof (see col.5 in US). See table I with one or two methyl groups permitted on piperazine ring carbons. Thus anisole (at instant B) compounds within claims 3 and 4 (and claims dependent thereon) are obvious variants of those taught by Chang in view of the equivalency teachings permitted at NR8R9 and R3-R5 in US Chang.See formula I, definition of all variables in cols.3-4. While Chang teaches up to 2 methyl groups on the piperazine carbons, the addition of an extra Me is not deemed a patentable advance absent

evidence of superior,unexpected results. Note In re Wood 199 USPQ 137; In re Lohr 137 USPQ 548; In re Fauque 121 USPQ 425.

Claims 1-3,16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Calderon and Bilsky references. Each of the 3 references discloses anisole derivatives instantly embraced for use in treating pain. In Calderon see compounds 8 and 9 in Scheme 2 and discussed elsewhere. Note Calderon teaches the same process as claimed herein. In the Bilsky references the anisole derivative is identified as SNC80 (see p.360) and as SNC67 (another enantiomer on p.25 of the Reg.Peptide reference).

Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Calderon,Bilsky references in view of Chang (US'830). Closest compounds in claims 4 and 5 (and claims dependent thereon) are HCl salts and with an additional methyl group on the piperazine ring. See compounds 58 and 60 in claim 4. Chang teaches salt forms including the hydrochloride salts as discussed in col.5. While Chang teaches up to 2 methyl groups on the piperazine ring the addtion of an extra Me group is not deemed a patentable ad vance for reasons given in the above 103 rejection over Chang.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1,2,4,5,16 and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 6,130,222. Although the conflicting claims are not identical, they are not patentably distinct from each other because the narrower subject matter covered by the claims in the US patent are also embraced herein as instant case is a continuation of US'222.

Claims 1-5,16 and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 6,680,321. Although the conflicting claims are not identical, they are not patentably distinct from each other because they embrace overlapping subject

matter when instant A is 1st formula in claim 3 with all other variables covered by the claims in the US patent also embraced herein. US'321 is also a continuation of instant case.

Claims 1,2,5,16 and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 6,696,447. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter covered by the claims in the US patent (which has a later effective filing date) has species that anticipate the instant claims.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned 6,696,447, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

All non-commonly assigned references applied above have been provided in earlier parents and have been cited by applicants in their IDS filed 11/17/03.

The list of commonly assigned applications indicated on p.1 of the IDS statement have been considered. One of these corresponds to US'447 made of record by the examiner as well as recent parent, US'321.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is (571) 272-0664.

If attempts to reach the examiner by phone are unsuccessful, the supervisor for AU 1624, Dr. Mukund Shah, can be reached at (571)272-0674.

The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

E Bernhardt

EMILY BERNHARDT

PRIMARY EXAMINER

Group 1600